



CIRM Shared Research Laboratory Information Form – Part Two

Section A. Project Information

Project Title The University of California San Francisco Shared Research and Teaching Laboratory: a Non-Federal Human Embryonic Stem Cell Resource for the Bay Area Community

Limited to 300 Characters

Project Start Date Jul 1, 2007

Construction Start Date Oct 29, 2007

Occupancy Date Aug 22, 2008

Total Part Two Funds Requested for Shared Laboratory Space \$1,999,692

Total Part Two Funds Requested for Stem Cell Techniques Course \$ 499,956

Total Capital Funds Requested \$1,349,127

Note: All green fields are calculated values. Do not enter a value in the field.

Please indicate whether you propose to apply for funding of a Stem Cell Techniques Course along with the Shared Laboratory Space, or just the Shared Laboratory Space.

☐ Shared Research Laboratory only

☒ Shared Research Laboratory and Stem Cell Techniques Course

NOTE: Please be aware that any information you provide in this form will be made publically available.

Section A. 1. Program Director

Name	Dr.	Linda	C.	Giudice	
	Prefix	First	Middle	Last	Suffix
Email (office)	giudice@obgyn.ucsf.edu			This email address identifies you to CIRM. Please use this email address for all correspondence with CIRM.	
Application Number	CL1-00523-1			This field should fill automatically, based on the email address. If not, enter the number you received via email from CIRM, in the form "XX9-99999-9", where "X" is a letter, and "9" is a digit.	

Section A. 2. Facilities Contact

Name	Mr.	Michael		Bade	
	Prefix	First	Middle	Last	Suffix
Institution	University of California, San Francisco				
Other Institution	If your institution is not listed, please identify the name of the institution here.				
Position Title	Director, Capital Programs				
Department	Capital Projects & Facilities Management				
Address	3130 20th Street				
	Box 0894				
City	San Francisco			CA	Zip Code 94143
Phone Number	(415) 502-6460		Ext	Fax Number (415) 476-6503	
Email (office)	mbade@fm.ucsf.edu			This email address identifies you to CIRM. Please use this email address for all correspondence with CIRM.	



CIRM Shared Research Laboratory Information Form – Part Two

Section A. 3. Public Abstract

See Appendix A.

Section A. 4. Statement of Benefit to California

See Appendix A.



CIRM Shared Research Laboratory Information Form – Part Two

Section B. Laboratory Renovation Plan

Project Manager	Ms. Patti Mitchell	Construction Supervisor	TBD
Title	Project Manager	Title	
Company/Institution	UCSF, Capital Programs	Company/Institution	

Describe plans for development/renovation of the shared laboratory space including fixed equipment costs. Include a description of the current space and how it will be renovated and reconfigured to form the laboratory. Include as attachments one 11x17 page of the current floor plan space and one 11x17 page of proposed floor plan of the renovated space. Describe all renovations that will be done. Describe how the project will be managed and tracked, as well as how change orders will be handled. For laboratories that are proposed to be located in leased space, provide information regarding the institution's long-term access to the leased space. Describe plans and schedule for all phases of development including design, construction, and installation of equipment leading to a functional laboratory. Give a proposed contingency plan in case of cost overruns. Any additional costs due to budget overruns will be the responsibility of the grant recipient. **(narrative limited to 3 pages)**

1. Summary of Part 1. In the first part of this application, we proposed to create a CIRM Shared Research Laboratory (described in this section) that includes a teaching component (described in Section C). Our goal is to ensure that investigators at the University of California, San Francisco (UCSF) and neighboring institutions have access to the highest-quality nonfederal human embryonic stem cell (hESC) lines and the specialized equipment required to study them. UCSF and Drs. Linda Giudice (Program Director) and Susan Fisher (Associate Program Director), both with established hESC programs, are deeply committed to advancing hESC research. We believe that promoting the highest-quality basic science research governed by a sound ethical framework is the fastest route to devising therapies for human diseases.

Part 1 of this application described UCSF's long history of work in stem cell research, which enables us to bring unique resources to this project. In particular, our applicant team has a great deal of experience in helping researchers grow hESCs and use them as experimental tools. In 2002, UCSF was awarded a federal grant for distribution of the HSF-1 and -6 lines, which are on the federal registry. Mr. Juanito Meneses, a member of our team, played an integral role in the derivation of these lines and has been an important contributor to the techniques course that is part of this effort. We also have other unique resources, such as a large bank of nonfederal hESCs. Thirteen of these lines were produced by investigators on this application, specifically, Dr. Fisher's group along with Mr. Meneses, since the federal registry closed in 2001. We will also obtain hESC lines from our collaborators at other institutions. Note that we are currently working closely with the UCSF Stem Cell Research Oversight (SCRO) committee, of which Drs. Giudice and Fisher are members, in developing suggested guidelines for using hESC lines derived elsewhere, paying particular attention to issues related to the protection of human subjects. Our collaborators include Dr. Outi Hovatta (Karolinska University Hospital, Sweden), who will provide us with four lines, and Dr. Carlos Simon (Banco Nacional de Lineas Celulares, Valencia, Spain), who will send us three more.

In Part 1 we also explained the need for a shared facility that will be used by our UCSF colleagues and hESC researchers at neighboring institutions. UCSF was awarded a CIRM training grant in 2006, which supports 16 graduate students, postdoctoral fellows and clinician scientists. We are committed to facilitating their work. Additionally, UCSF investigators, including Dr. Giudice, recently received eight SEED grants; one decision is pending and six comprehensive applications have been recommended for funding with Dr. Fisher's grant among them. Thus, we already have a large user base, with many other investigators at our institution showing a great deal of interest. Furthermore, we included letters in our proposal from scientists at 10 neighboring institutions (e.g., UC Berkeley and San Francisco State University) who want to work or take classes in our facility.

Finally, in Part 1 we described our vision for how the Shared Research Laboratory will be run under the purview of our oversight committee, which will set priorities. We believe it will be feasible to meet the needs of our large user base because UCSF has developed a mechanism for allotting additional space in the laboratories of individual PIs to be used for nonfederal hESC research. This mechanism allows projects to transition out of the shared facility once investigators develop nonfederal areas in their own labs. We believe that funding from CIRM grants will greatly facilitate the process of equipping these areas. As projects exit, we will bring in new groups with the guidance of the oversight committee. Thus, we envision the CIRM Shared Research Laboratory as a hub, with the spokes being nonfederal areas in the labs of PIs at UCSF and other institutions, who will use our equipment on an ongoing basis. We think that this model will be adopted by our users at neighboring institutions.

2. Existing Building. We now detail our plans for construction of a CIRM Shared Research Laboratory that will be housed in the southwest corner of the 16th floor of the east tower (HSE-16) of the Health Sciences Instructional Research (HSIR) towers on the UCSF Parnassus Heights campus. This tower is one of a chain of interconnected buildings that serve the campus's teaching, research, and patient care missions. The other basic science laboratories of the School of Medicine are located on this and neighboring floors of the HSIR towers, the adjoining Medical Sciences Building, and the Clinical Sciences Building. The proximity to colleagues within the Schools of Dentistry, Pharmacy, and Nursing, contributes to a collaborative and interactive atmosphere.

The HSIR towers, built in 1968, were designed with a perimeter corridor and free span open laboratory spaces between the



CIRM Shared Research Laboratory Information Form – Part Two

Section B -- 1. Laboratory Renovation Plan (continued)

perimeter columns. HSE-16 is entered and exited through the northwest corner of the north side, through a corridor housing elevators and restrooms, in the lobby between the HSIR towers. An exit stair tower is located on the east side of the building. The mechanical system is fed from the east side of the building through four main ducts that decrease in size as they travel west. The heating, ventilation and air-conditioning, lighting and main utilities are fed diagonally through the ceiling. The existing laboratory dates from the original build-out of the floor (see Attachment 1, which includes photos). It is divided into offices, a darkroom with sinks, open laboratories and closed laboratories. The inner boundary of the existing columns forms the outside limits of the laboratory walls.

In 2005-2006 the north and west portions of the floor were renovated into the Human Development and Stem Cell Research Center. This project created two separate entities. One entity is laboratories for federally funded research (shaded in red on Attachment 1). Dr. Fisher, the Associate Program Director, and her group occupy the northwest corner of this area. This project also created a laboratory for nonfederal research that utilizes human gametes and embryos. Currently this area is heavily used by our applicant team. The nonfederal area was remodeled with funds from the dean's office (School of Medicine) and the Institute for Regeneration Medicine (Dr. Arnold Kriegstein, Director). The 1,147 sq. ft. space is in the Department of Obstetrics, Gynecology and Reproductive Biology, chaired by Dr. Giudice, the Program Director. This area, shaded in blue on Attachment 1 (with a portion enlarged in Attachment 2), includes a NONFEDERAL SHARED EQUIPMENT ROOM with a fume hood, an open NONFEDERAL LAB, two NONFEDERAL IMAGING ROOMS that contain microscopy equipment for close examination of cells, a NONFEDERAL TISSUE CULTURE ROOM that also houses the UCSF HUMAN GAMETE AND EMBRYO BANK and an interior room (MICROMANIPULATION) that contains highly specialized equipment for manipulating single cells and embryos. Across the hall, two imaging rooms that were renovated at the same time (124 sq. ft.) contain additional microscopy equipment—a fluorescence microscope and a time-lapse videomicroscopy system. This previously renovated space is fully occupied by ongoing projects. The entire nonfederal area and the equipment it contains will be available to users of our proposed Shared Research Laboratory. Faculty offices that house personnel who will play key roles in this project are easily accessed from the central corridor on the west side of the floor. A preexisting conference room and a break room are located on the east side of the floor plate.

The area to be remodeled, which has asbestos fireproofing on the steel beams, has been surveyed and documented. Based on several other projects in these buildings, the hazardous material can be removed within 3-5 weeks during the demolition phase.

3. Proposed Shared Research Laboratory. Our existing nonfederal laboratory was not designed as a shared research (or teaching) facility. The intent was to support somatic cell nuclear transfer and research involving human gametes and embryos. Therefore, we are woefully short of the specialized lab space that is needed to grow, propagate, derive and analyze nonfederal hESCs. In this context, we request funds to renovate an adjacent lab for this purpose. The new CIRM facility, 1311 sq. ft., will adjoin the nonfederal laboratory at the common equipment room (see Attachment 2). The construction will extend to the outside face of the existing columns. The entire plan, to be built if funds for both the Shared Research Laboratory and the Teaching Laboratory effort are awarded, includes a suite of three hESC growth and propagation rooms, one of which will also be used for hESC derivation. These rooms will be entered through a common gowning room where researchers will don coats, head covers and booties, a practice that helps keep the inner rooms free of contamination. In addition, there is a significant amount of open bench space and an area for the fluorescence-activated cell sorter (FACS) we are proposing to purchase, which allows isolation of hESC subpopulations. The portions that will be built with funds for the Shared Research Laboratory, 698 sq. ft., are shown in blue font on Attachment 2. The budget (see Section B.2) includes demolition of the entire space and creation of a NONFEDERAL DERIVATION/hESC GROWTH & PROPAGATION RM, NONFEDERAL hESC GROWTH & PROPAGATION RM 1, and GOWNING room. Additional spaces (613 sq. ft.), shown in green font, will be created if the teaching effort is funded (see Section C.2). These include NONFEDERAL hESC GROWTH & PROPAGATION RM 2, a "TEACHING GREEN" DISCUSSION/INTERACTION AREA, and a SHARED TEACHING LABORATORY.

To a certain extent, the building code guides the layout of the spaces. We will take advantage of the exit at the equipment room as the secondary exit from the suite, through the nonfederal equipment room to the west corridor; our primary exit will be to the south (up sheet). The building code requires that a laboratory > 200 sq. ft. have its own secondary exit directly to the exit corridor. The NONFEDERAL DERIVATION/hESC GROWTH & PROPAGATION RM and NONFEDERAL hESC GROWTH & PROPAGATION RM 1 are entered through GOWNING. With the approval of UCSF Environmental Health and Safety, we are providing a single hand wash sink and an emergency eye wash station for rooms in the gowning area. This is at the request of the scientists to reduce possible sources of contamination, such as sinks, in the rooms where hESCs and human embryos will be handled.

NONFEDERAL hESC GROWTH & PROPAGATION RM 1, named for the activities that will take place in this area, will have a second, emergency-only exit directly to the corridor to the south. This emergency exit will be air-penetration-gasketed to maintain the positive pressure in the room and will have no exterior hardware facing the corridor. This room will house three 4-ft. nominal vertical biosafety hoods and three double stacks of incubators for nonfederal hESC growth and propagation. Additionally, this room will have its own large "deli-style" refrigerator with sliding doors. The space between the hoods and the incubators on the opposite wall is more generous (> 5 ft. 3 in.) than that typically allotted in a room used for growing cells, and



CIRM Shared Research Laboratory Information Form – Part Two

Section B -- 1. Laboratory Renovation Plan (continued)

will accommodate several scientists working at the same time. We note that the airflow to this room is specially designed to prevent microbial contamination that could occur due to higher than normal rates of occupancy. The size of this room also makes it completely accessible and compliant with the Americans with Disabilities Act (ADA).

The smaller room in the center is designated on the plan as NONFEDERAL DERIVATION/hESC GROWTH & PROPAGATION. The name reflects our intention to use this area for two purposes. First, the design accommodates hESC growth and propagation. Second, we intend to exploit the unique expertise of our personnel to continue deriving new hESC lines, procedures that we will also teach. This area will have two double stacks of incubators and two horizontal embryo hoods, which can also be used for hESC growth and propagation. Additionally, the room will contain a dual-height cabinet. The bench space will be dual level to accommodate an under-counter freezer and an under-counter fridge. A portion of the bench, which will be positioned at sitting height, will also have a knee hole for microscope use. Please note that this room is also ADA compliant.

Just outside the south door is an enclosed room that will house the gas tanks required for the incubators in the suite. Gases will be distributed to the rooms and run through a manifold that will notify personnel of gas usage and level. By locating them just outside the suite, we eliminate "unauthorized" access during tank replacement.

The newly designed Shared Research Laboratory will be connected to the current nonfederal lab through a NONFEDERAL SHARED EQUIPMENT ROOM. This allows for common use of the freezers, fume hood, and other equipment housed therein, and easy access to the existing nonfederal space, shaded in blue, described in section 2 above. The proximity of the existing offices, break room and conference room will foster collegial interactions.

Finally, we note that entry to the entire HSE-16 floor is restricted by Cardtrol access, which also records the name of the individual who enters the space. Additional card readers are installed at the two entrances to our existing nonfederal space, of which the west corridor door will be the primary entrance to the newly renovated lab space. Ms. Meagan Cron, head administrator of the Center for Reproductive Sciences (Department of Obstetrics, Gynecology and Reproductive Sciences), whose office is adjacent to the nonfederal space, will have sole responsibility for issuing cards after checking that the appropriate approvals have been obtained. In addition, she will document that the user is a scientist from a California institution.

4. Project Management and Tracking. The project will be managed internally by the UCSF Capital Programs and Facilities Management Department. The project manager, Ms. Patti Mitchell, will take the project from conception through occupation. The architect will refine the plan submitted, working with his/her engineers on the mechanical and electrical design for the suite. There will be design sign-off meetings with the anticipated occupants to minimize design changes to the plans during the construction phase. The schedule for the design phase will include a demolition package and a construction package. The demolition package will be available for bid around September 17, 2007, and the construction package will be available in late December. Because the project manager is already familiar with the building from the previous HSE-16 lab renovation, we feel that an aggressive schedule is feasible for this project.

The project will be reviewed internally for compliance with the Facilities Guidelines at 100% Design Development, 50% Construction Documentation and 95% Construction Documentation. In addition, this project will require review and approval by the California state fire marshal for code compliance and the Division of the State Architect for compliance with ADA. UCSF is a self-permitting facility so will not require review, approval or permitting by the city of San Francisco.

Once the documents are approved, they will be publicly advertised for bid. As indicated above, we will bid this project in two phases. Due to the immediate availability of the designated space, we will split the overall construction time into a demolition phase and a construction phase. We will be able to start the abatement and demolition much earlier and improve the overall schedule by using this approach. The architect and engineer will then have an opportunity to view the clean shell during the construction documentation phase and incorporate any unique conditions not previously identified during site visits to the existing lab space. We will provide a walk-through of the demolished lab as part of the bid process for the construction phase. In previous projects, this approach has been proven to reduce overall bid duration by minimizing the number of clarifications and addenda, as the above ceiling area is visible to the potential contractors, abandoned utilities have been removed, and a less congested space is available to the potential general contractors and subcontractors.

Schedule and budget will be tracked through weekly construction progress meetings. This provides the opportunity to identify issues before they become critical and to resolve them without the undue pressure of schedule delays, which typically translate to added cost. We will track submittals, requests for information, and cost proposals with logs updated on a weekly basis.

Change orders will also be reviewed at these meetings. In previous projects where demolition occurred before awarding of the construction contract, we have seen an ~1% change order impact to the construction budget. The cost is absorbed by the contingency so has no overall effect on the project budget.

After the layout and framing are complete, the architect will confirm locations of back boxes for power, phone and data, along with sink and other plumbed requirements, with the construction documents. He/she will also review these locations with the occupants to confirm that the equipment identified in the documents is valid and correct utilities are provided. This will minimize costly changes near job completion. At that time we will also work with the occupants to verify equipment ordered and to



CIRM Shared Research Laboratory Information Form – Part Two

Section B -- 1. Laboratory Renovation Plan (continued)

confirm delivery dates.

Within a few months of construction completion, around the end of June, 2008, we will begin working with the program directors, their personnel and assistants to coordinate delivery and/or installation of the phones, data, equipment and furniture as well as the actual move. UCSF's Telephone and Data Department will need locations of assigned personnel for relocation of their phone numbers and IP addresses. We will confirm schedules of these moves with the department of Obstetrics, Gynecology and Reproductive Sciences. Ms. Meagan Cron will be the point of contact. Our relocations manager will start coordinating delivery dates of new and existing equipment and furniture from their current locations to the Shared Research Laboratory.

Once the project has reached substantial completion, around August 22, 2008, and commissioning is under way, the contractor will provide the necessary training to the occupants of the lab and the UCSF Facilities personnel for the nuances of the renovated suite. Confirmation of the equipment and furniture deliveries and the physical move will be completed, and the actual move will commence.

5. Contingency Plan for Cost Overruns. In the case of construction bid overruns, Dr. David Kessler, Dean of the School of Medicine, will augment the funding as required to build the laboratories. A letter from Dr. Kessler attesting to this commitment, which was included in Part 1 of this application, is appended to our Part 2 submission.





CIRM Shared Research Laboratory Information Form – Part Two

Section B. 1. Schedule/Timeline and Drawdown of Funds Table

Provide a realistic schedule and drawdown of funds for completing each activity/milestone, as indicated below.

#	Activity/Milestone	Start Date	Completion or Milestone Date	Amount of CIRM funds to be drawn
1	Grant Award (estimate)		Jul 1, 2007	
2	Request for Planning Funds (10% of Construction Costs)		Jul 1, 2007	\$ 99,990
3	Prepare Preliminary Plans	Jul 9, 2007	Sep 10, 2007	
4	Approval of PPs		Sep 21, 2007	
5	Prepare Working Drawings	Sep 24, 2007	Dec 14, 2007	
6	Approval of WDs		Jan 11, 2008	
7	Request Construction Contract funds (80% of Construction Costs)		Dec 7, 2007	\$799,922
8	Advertise for Construction Contract	Jan 28, 2008	Feb 29, 2008	
9	Award Construction Contract		Mar 10, 2008	
10	Construction Activities	Mar 17, 2008	Aug 22, 2008	
11	Completion of Equipment Purchases		May 26, 2008	
12	Request Equipment Purchase funds		Jun 23, 2008	\$999,789
13	Beneficial Occupancy		Aug 22, 2008	
14	Notice of Completion		Aug 25, 2008	
15	Request Construction Completion Amount (10% of Construction Funding)		Sep 2, 2008	\$ 99,990

"Preliminary Plans" (PPs) represent approximately 35 percent of the design effort, or may be considered the product of completing the "Design Development" (DDs) phase of architectural work.

"Working Drawings" (WDs) represent drawings and specifications from which a contractor may determine the full extent of work contemplated in the project for purposes of submitting a bid; may be referred to as completion of "Construction Documents" (CDs) phase of architectural work.



CIRM Shared Research Laboratory Information Form – Part Two

Section B. 2. Budget

Provide a complete budget for the renovation that includes construction costs, design fees, administration of the project, other costs (i.e. installation of equipment) and a construction contingency (limited to 7-10% of the construction budget). Identify the amount of CIRM funds requested and the matching funds (construction requires 20% matching funds). Provide a complete budget for movable equipment (equipment requires 20% matching funds). (narrative limited to 3 pages)

(Note: An Excel spreadsheet can be attached as long as the total submission for this Section is limited to 3 pages)

1. RENOVATION BUDGET. Overview. We are requesting funds to demolish 1311 sq. ft. of existing space and renovate the portion of the project (shown in blue font on Attachment 2) that will comprise a NONFEDERAL DERIVATION/hESC GROWTH & PROPAGATION RM, NONFEDERAL hESC GROWTH & PROPAGATION RM 1 and GOWNING area. The names of the rooms denote the activities they will house. Our highest priority is enabling growth and propagation of nonfederal hESC lines, but we also want to exploit the unique expertise of our team to continue deriving new hESC lines. The rest of the space will be shelled out, creating the corridor and exits required by code. Since demolition and shelling out are part of the Shared Research Laboratory project, the per sq. ft. costs are higher than those for the Shared Teaching Laboratory. The newly renovated space will be physically connected to our existing nonfederal laboratory (shaded in blue on Attachment 2) through an equipment room. Therefore, the CIRM facility will be physically integrated with a fully functional research lab that houses complementary activities.

The spaces labeled on Attachment 2 reflect our vision for optimal use of this lab, i.e., integration of our research (blue font) and teaching (green font) activities. We have been helping investigators incorporate hESC approaches into their work for 5 years. Thus we already have a workable system in place (described in section C of this application). In addition to formal courses and to remove delays that are inherent in adhering to course schedules, we teach hESC techniques on an informal, "learn as you go" basis. This type of learning experience is also the best way to teach other investigators how to derive hESCs. Building the entire project will allow us to use all of the space all of the time for both research and teaching purposes.

- Itemization and Justification. Our proposed budget for the Shared Laboratory is detailed in Attachment 3. Line items are color-coded and map to the categories listed in the Budget Summary Table (see legend at the bottom of the page). Together, the two budgets give a detailed breakdown of our project costs.

Many factors contribute to this bottom line. Renovation projects in the San Francisco Bay Area, and at UCSF in particular, face unique constraints: (i) Relatively high labor rates. (ii) A scarcity of qualified subcontractors, especially electrical, partly because of competition from the information technology and biotechnology industries in the region. (iii) At the Parnassus Heights campus: (a) There is no space available for storage of construction materials, which must be delivered on an as-needed basis. (b) Parking spaces are at a premium; contractors are forced to pay for parking at very high rates, coordinate off-site parking and shuttle services, or schedule arrivals during off-hours at higher labor rates. (c) The loading dock and freight elevators are overutilized due to the many construction projects under way on campus; because debris removal and deliveries must be coordinated, every contractor is forced to accept an equal share of off-hours work. (d) Because this project involves renovation rather than new construction, disruption of ongoing research in adjacent areas and floors must be kept at an absolute minimum: utilities for laboratories in the vicinity must be maintained, and interruptions must be limited to short spans of time. These restrictions often entail out-of-sequence work and, again, higher costs. (e) The facility is aging. Asbestos used in fireproofing the structural members must be replaced before new utility systems can be installed. The relocating and running of utilities takes a sophisticated degree of coordination to work within the existing beam penetrations of HSE-16. Thus, only the most experienced heating, ventilation and air-conditioning subcontractors are qualified to renovate research laboratories within this building.

Given the challenges of working on the Parnassus Heights campus, how can we achieve cost containment? The simple answer is experience. We have an extremely experienced project manager, Ms. Patti Mitchell, who has worked for the UCSF Capital Programs and Facilities Management Department for 3 years. To date she has assisted in or taken charge of sixteen renovations, including management of the 2005-2006 HSE-16 project that renovated our current federal and nonfederal labs (see Attachment 1). Furthermore, she has been involved with several large-scale projects in the HSIR towers, including gutting and renovating the entire 6th floor of the west tower (HSW-6). We note that the Associate Program Director, Dr. Fisher, was part of both the HSE-16 and HSW-6 projects. Thus, our project team includes individuals with a great deal of experience working together. Therefore, we will be able to move efficiently through all phases of the renovation and deliver the project on time and on budget.

- Institutional Match. Since 2005, the UCSF School of Medicine has contributed \$518,000 (see letter from Dean David Kessler), and the Institute for Regeneration Medicine has donated \$560,000 (see letter from Director Arnold Kriegstein), which funded the creation of our existing nonfederal laboratory (see Section B.4, Institutional Commitment). For application purposes, we assigned two-thirds of this amount, \$711,000, to the Shared Research Laboratory portion of the application.

- Benefit to California's Economy. We will choose an architectural firm and a contractor that are California-based businesses.

2. MOVABLE EQUIPMENT. Overview. We propose to purchase (i) movable equipment required to outfit the rooms that will be constructed if we are awarded the Shared Research Laboratory grant (shown in blue font on Attachment 2), e.g., tissue culture hoods, incubators and related equipment for growing and propagating nonfederal hESC lines; and (ii) major equipment consisting of more expensive items with specialized functions, e.g., a fluorescence-activated cell sorter (FACS), which will allow



CIRM Shared Research Laboratory Information Form – Part Two

Section B. 2. Budget (continued)

us to separate hESCs and their differentiated products according to sets of individual molecular properties, and a videomicroscopy set-up, a powerful tool for studying the behavior of hESCs.

- Itemization and Justification. We are requesting \$999,789 to purchase equipment. Due to space constraints, the total cost plus tax (but not per unit values) is presented for each type of equipment in the narrative, rather than in tabular form. Most items (shown in blue font) are placed on Attachment 2, in the space it will occupy. Since this is a multiuser research laboratory, we will need to purchase pieces of equipment in sufficient quantity to allow several investigators to work simultaneously.

The purchase of five tissue culture hoods is crucial to our ability to grow hESCs and embryos. To be sure that airborne microbes do not infect our cells, which are grown without antibiotics or anti-fungals, we work in specially designed boxes with glass barriers that strictly regulate airflow. The two embryo and hESC tissue culture hoods (\$19,806) will be located in the NONFEDERAL DERIVATION/hESC GROWTH & PROPAGATION RM. They are specially designed to accommodate a microscope with which to magnify images of embryos and hESCs up to 100 times. The three hESC tissue culture hoods (4 ft.), to be used in NONFEDERAL hESC GROWTH & PROPAGATION RM 1, have a standard design in which the glass barrier rolls up (\$26,520).

We plan to purchase 10 hESC tissue culture incubators, which can be stacked (\$89,400). Two double stacks (e.g., 4 incubators) will be located in the NONFEDERAL DERIVATION/hESC GROWTH & PROPAGATION RM and three (e.g., 6 incubators) in the NONFEDERAL hESC GROWTH & PROPAGATION RM 1. These devices are designed to mimic the temperature, humidity and oxygen content of the human body, and they have double doors that strictly control the inner environment. We are buying a particular type of incubator that will allow us to raise or lower oxygen levels: Standard incubators deliver only 20% O₂, whereas embryos, hESCs and their derivatives, depending on their proximity to blood, experience 2-20% O₂. Creating culture conditions that are as realistic as possible is crucial to regulating cell behavior.

Microscopes are key tools for hESC researchers. The two dissecting microscopes we plan to purchase are specially configured to allow viewing and simultaneous manipulation—e.g., when separating the cells that form hESCs from the rest of the embryo, or when mechanically dividing groups of hESCs termed colonies (\$43,577). One microscope has a camera for record keeping. We also need a phase-contrast microscope (with camera), which alters the light path to create the contrast needed to see details at a cellular level (\$48,078). The NONFEDERAL hESC GROWTH & PROPAGATION RM 1 will also have a phase-contrast microscope with camera and fluorescence, to allow observation of genetic tags that we introduce into hESCs (\$105,550).

hESC derivation, propagation and growth require a large number of specialized solutions that for reasons of chemical stability must be kept cold or frozen. The NONFEDERAL DERIVATION/hESC GROWTH & PROPAGATION RM will have an under-counter refrigerator (\$748) and freezer (–20o Celsius; \$748). The NONFEDERAL hESC GROWTH & PROPAGATION RM 1 will have a full-size “deli-style” refrigerator (\$3,600) and a full-size, upright freezer (–20o Celsius; \$1,045). The larger units will accommodate the needs of the multiple investigators who will work in this room. Installation of refrigerators and freezers in each room reduces foot traffic and the possibility of microbial infection. Finally, we want to purchase a large, upright –80o Celsius freezer (\$12,572), because some chemicals and biologicals degrade at higher temperatures; it will reside in our existing equipment room.

The controlled-rate freezer (\$15,158) and the Cryosafe (\$9,959) are used for frozen storage of hESCs. The controlled-rate freezer allows us to fine-tune the exact cooling conditions for each cell line, which in turn, enhances their ability to regrow after the freezing process. The Cryosafe cools cells to several hundred degrees below zero, the preferred method of long-term storage. We need the computer and the software (\$5,000) to track where cells and samples are stored, particularly important given the number of users who will be working in our Shared Laboratory Facility. Finally, each room will contain a centrifuge (\$26,304 total cost for two) that rapidly spins cells in solution. This process, which uses the force of gravity to pull cells to the bottom of a tube, enables isolation of hESCs and other cell types.

We also request funds to purchase two specialized pieces of equipment. A FACS instrument is an essential tool for hESC researchers (\$486,662). Typical applications include separating differentiated from undifferentiated cells and interrogating the molecular composition of cells. We plan to place this piece of equipment in the new SHARED TEACHING LABORATORY. If this renovation is not funded, the FACS machine will reside in our current nonfederal lab.

Finally, we request funds for a second videomicroscope (\$105,062) for taking close-up movies of our cells, which give us key pieces of information that we cannot acquire in other ways. In science, as in other elements of life, a picture is worth a thousand words and a movie contains even more valuable information. To prevent vibration, it sits on an air table. The videomicroscopy unit we already own is running at full capacity. With so many new users, we need to duplicate this item. One of the imaging rooms in our current nonfederal space was specially designed for this equipment.

- Institutional Match. Since 2005, the UCSF School of Medicine has contributed \$283,628 for the purchase of key equipment that is housed in our current nonfederal space. The School of Medicine provided \$74,402 for acquisition of the specialized equipment that enables the micromanipulation of gametes and embryos (see appended letter from Dean Kessler). The Institute for Regeneration Medicine donated \$209,226 (see appended letter from the Director, Dr. Kriegstein), which enabled purchase of



CIRM Shared Research Laboratory Information Form – Part Two

Section B. 2. Budget (continued)

a confocal microscope that allows us to take pictures of labeled molecules deep inside cells and assemble these pictures into three-dimensional reconstructions. The details of these financial investments are given in Section B.4 (Institutional Commitment). As with the match for renovation dollars, these funds were arbitrarily split between the research and teaching portions of this application, with two-thirds, \$187,194, assigned to the former.

- Benefit to California's Economy. We will make every effort to purchase equipment from CA-based companies. For example, the Bioscience Division of Becton Dickinson, from which we will purchase the FACS machine, is based in San Jose, CA.



CIRM Shared Research Laboratory Information Form – Part Two

Section B. 3. Budget Summary Table

Complete the budget summary for the use of CIRM funds.

Note: All colored fields contain calculated data. Please do not enter anything in those fields.

Other Project Costs				
Budget Category		Total Budget	CIRM Grant Funds	Institutional Match
Construction Contract Costs		\$ 627,831	\$ 627,831	\$ 000
Other Construction Costs (institutional)		\$ 67,173	\$ 67,173	\$ 000
Subtotal Construction		\$ 695,004	\$ 695,004	\$ 000
Design Fees		\$ 141,431	\$ 141,431	\$ 000
Administrative Costs		\$ 102,445	\$ 102,445	\$ 000
Construction Contingency		\$ 61,023	\$ 61,023	\$ 000
Total Construction		\$ 999,903	\$ 999,903	\$ 000
Movable Equipment		\$ 999,789	\$ 999,789	\$ 000
Total Budget		\$1,999,692	\$1,999,692	\$ 000
Gross Square Feet	698	\$1,432.53	\$1,432.53	Const Costs/GSF
Assignable Square Feet	631	\$1,584.63	\$1,584.63	Const Costs/ASF



CIRM Shared Research Laboratory Information Form – Part Two

Section B. 4. Institutional Commitment

Provide a detailed description of the amount and source of matching funding for each request that requires matching funds. The requirement of matching funds can be satisfied if the institution can document funds, excluding other grant funds, committed to similar projects (i.e., renovation of lab space and equipment purchase) after January 1, 2005. Detail the use of the space after the three year period is completed. (narrative limited to 2 pages)

1. Institutional Commitment Before 2005. Although we were asked to provide information dating from 2005, we note that UCSF has a long history of investing both intellectual and financial resources in nonfederal hESC research. Starting in 1997 this institution supported the work of Dr. Roger Pedersen's group, one of whose members, Mr. Juanito Meneses, is now a member of our applicant team. They were working in what was then a nonfederal mode to derive the first hESC lines. Although they did not win this race, they were ultimately successful. Therefore, in 2001 UCSF was able to contribute two hESC lines (HSF-1 and -6) to the federal registry. In 2003, the School of Medicine provided \$1.3 million as start-up funds for the newly created Human Embryonic Stem Cell Program, of which Dr. Susan Fisher is the Acting Director. Finally, in 2004, the Institute of Regeneration Medicine, headed by Dr. Arnold Kriegstein, was created with \$11 million in funds contributed by the School of Medicine and a group of highly committed donors. This investment resulted in the recruitment of eight additional, primarily junior faculty members to UCSF to work on important aspects of stem cell biology. Thus, UCSF has been making substantial investments in hESC research for over 10 years.

This institution is also heavily invested in the important process of developing ethical standards for work in this field. The faculty leaders who have been involved in this process are members of the oversight committee that will govern the operations of our Shared Research (and, if awarded, Teaching) Laboratory. This committee will be chaired by Dr. Keith Yamamoto (Executive Vice Dean, UCSF School of Medicine). Dr. Yamamoto, a member of the National Academy of Sciences, has been a major proponent of nonfederal hESC research at UCSF and has published articles on ethical aspects of this work. The oversight committee will also include other colleagues well versed in ethical issues surrounding hESC derivation and research. Dr. Elena Gates (Professor, Department of Obstetrics, Gynecology and Reproductive Sciences) and Dr. Bernard Lo (Professor, Department of Internal Medicine) have defined parameters that should be considered in obtaining informed consent for gametes and embryos to be used in hESC research. Along with co-author Dr. Yamamoto, they have published their conclusions as high-profile scientific articles.

Additionally, Dr. Giudice, the Program Director and a member of the Institute of Medicine (IOM) of the National Academy of Sciences, led an IOM workshop supported by the CIRM and recently published a report on "Assessing the Medical Risks of Human Oocyte Donation for Stem Cell Research" (http://books.nap.edu/openbook.php?record_id=11832&page=R1).

2. Institutional Commitment After 2005. The dollar amounts expended for renovation and equipment since 2005 are detailed in Table I. With regard to renovation, the Dean's office (School of Medicine) contributed \$518,000 and the Institute for Regeneration Medicine (Dr. Arnold Kriegstein, Director) contributed an additional \$560,000 for remodeling of 1,147 sq. ft. of space in Dr. Giudice's department to create our existing nonfederal laboratory. This entire area and the equipment it contains, which is used for somatic cell nuclear transfer and research involving human embryos, will be available to users of our proposed Shared Laboratory (and Teaching) Facility. This is in addition to the similar-sized area that we propose to renovate if this application is funded, which will contain the specialized rooms that are required for hESC growth and propagation as well as derivation, along with additional areas for specialized research and teaching activities.

UCSF has also made recent investments in equipment that resides in our current nonfederal laboratory. Funds from the Dean's office (School of Medicine), \$74,402, were used to purchase a highly specialized piece of equipment that allows micromanipulation of single cells, e.g., human eggs, or collections of cells, such as those obtained for human embryos. Typical procedures include somatic cell nuclear transfer. The details of this purchase are shown in Table I. The various parts include a microscope that greatly enlarges images of these tiny cells. Other accessories include a micromanipulation package for moving single cells or nuclei, custom capillaries for transferring them, a heated stage that keeps the cells at body temperature, and the fluorescence option that allows us to work with genetically labeled cells. The entire system is computer controlled, which requires specialized software. We also have a camera and a computer, which allow us to keep photographic and written records of our experiments.

The largest equipment purchase was made with funds totaling \$209,226 from the Institute for Regeneration Medicine. We used this money to buy a confocal microscope, a key piece of equipment for hESC investigators. Specifically, this microscope allows a three-dimensional reconstruction of individual cells and groups of cells, such as hESC colonies, or their differentiated progeny, such as those that produce insulin. Being able to "see inside" cells is crucial for understanding how they function.



CIRM Shared Research Laboratory Information Form – Part Two

Section B. 4. Institutional Commitment (continued)

Several items of equipment are required for this sophisticated procedure (see Table I). These include the microscope itself and its confocal components. The associated optical systems include sources of transmitted light and equipment for generating fluorescence, which is used to observe protein and genetic materials with specialized tags that this equipment can image.

Table I. Institutional Commitment: Funds Expended For Renovation and Equipment Purchases.

CATEGORY/SOURCE	INSTITUTIONAL MATCH
Renovation:	
School of Medicine	\$518,000
Institute for Regeneration Medicine	\$560,000
Subtotal	\$1,078,000
Equipment:	
Micromanipulator	
microscope	\$ 36,383
micromanipulation package	\$ 29,265
custom capillaries	\$ 916
heated stage	\$ 2,969
fluorescence option	\$ 3,920
Image Pro Express software	\$ 949
Subtotal	\$ 74,402
Confocal Microscope	
microscope	\$ 26,353
confocal components	\$138,494
optical system (transmitted light)	\$ 19,514
fluorescence equipment	\$ 21,015
camera with computer	\$ 3,850
Subtotal	\$209,226
Total -----	\$1,361,628

3. Plan for Continued Operation Beyond the Initial Three-Year Period. The continued operation of the facility is ensured by our intent to transition to a recharge system. Initially, we will charge only the investigators who have budgeted for personnel costs and tissue culture supplies in grants funded by CIRM or other nonfederal sources. We expect that this user base will significantly expand with time, as we anticipate that our investigators will be very successful applicants. A recharge system helped finance hESC activities that were part of our federally sponsored hESC course. Thus, the administrative infrastructure is already in place.

In addition, the Associate Program Director, Dr. Fisher, has demonstrated experience in moving a core research laboratory from subsidized status to a recharge basis. She is the faculty director of the Biomolecular Resource Center (BRC) Mass Spectrometry Facility, a campus-wide core that was established in 2003 with funds to cover personnel and equipment costs for the first three years of operation, coincidentally the same time frame as this project. In 2006, the BRC unit, which is now significantly expanded, became fully self-supporting. She will use this valuable experience to manage the same process for the CIRM Shared Research Laboratory. Finally, the space to be used is allocated to the Department of Obstetrics, Gynecology and Reproductive Biology, of which the Program Director, Dr. Linda Giudice, is the chair. She is committed to using the newly renovated area for nonfederal hESC research for the lifetime of CIRM.



CIRM Shared Research Laboratory Information Form – Part Two

Section C. Stem Cell Techniques Course (if applicable)

Based on the information provided in Part One of the application describing the course, include a justification of the additional space required and additional equipment requested, if any. Include additional square footage and provide as an attachment one 11x17 page of the proposed floor plan of the renovated space. (narrative limited to 1 page)

1. Course Description. Our team has a long history of training researchers how to grow and propagate hESCs. In 2002, UCSF was awarded a federal grant for distribution of the HSF-1 and -6 lines, which were derived at this institution. Based on the practical knowledge that we gained teaching investigators how to work with these lines, we envision offering three types of learning experiences. First, we will give a formal core course that covers growth, propagation and analysis of nonfederal hESCs. This course is offered as an intensive 5-day experience because it is difficult for investigators to leave their laboratories for longer periods of time. Given four times a year to classes of eight students each, the course will consist of lectures, laboratory experiences and research seminars. Day 1 will focus on ethics, institutional approvals (e.g., filling out paperwork for the committees on human research), embryology, hESC feeders/substrates and hESC plating. In the laboratory portion, students will learn how to culture both hESCs and the carpet of feeder cells on which they grow. In subsequent sessions, they will practice these methods and learn increasingly sophisticated techniques. Day 2 will cover hESC propagation, analysis of colony morphology and cryopreservation. We will map strategies for constructing hESC and feeder cell banks, a process whereby aliquots of cells are frozen rather than being continuously passaged and therefore subject to change. Day 3 topics will include methods for evaluating markers of pluripotency, followed by preparation and analysis of embryoid bodies, which are collections of hESCs that have been allowed to differentiate. Day 4 will be devoted to karyotype analysis (counting chromosomes) and pathogen testing to keep cell lines microbe free. Day 5 will cover genetic modification and analyses that use fluorescence-activated cell sorting (FACS), a fundamental method for separating and analyzing hESCs. We will develop a Web portal to facilitate the course application process, distribution of teaching materials and communication with faculty. All students will be offered additional assistance in the form of protocols and one-on-one instruction after the 5-day session ends. We believe that continued consultation will ensure the students' future success.

We plan to offer two additional types of learning experiences: hESC derivation and informal training. Given our team's expertise in hESC derivation, we have an important opportunity to teach our methods to a small number of highly motivated investigators who are interested in producing additional, new and improved, hESC lines. For example, investigators at the Gladstone Research Institutes and UC Berkeley stated in their letters of support for Part 1 of our application that their scientists wanted to learn these procedures from us. In this case, the trainees will shadow laboratory personnel over many weeks as they carry out all aspects of the derivation process. This knowledge is not readily available, as the intricate lab techniques do not translate well to written form. Finally, we will teach researchers who use our CIRM Shared Research and Teaching Laboratory the elements of hESC culture on an informal, rolling basis. Rather than make completion of our core course a requirement for using the laboratory, we will teach individual users the particular elements of the curriculum that are applicable to their projects. We will encourage these "informal trainees" to attend our formal core course, particularly the lectures, which can accommodate a larger number of students than the laboratory portion. Thus, research and training activities will be going on continuously, side by side, a reflection of how an actual academic research laboratory functions.

2. Justification for Space and Equipment. UCSF investigators have a long history of being at the forefront of scientific revolutions. The hESC field is a prime example. We have a CIRM training grant, directed by Dr. Fisher, that supports 16 individuals. Additionally, UCSF faculty members received eight CIRM SEED grants, one decision is pending, and another six COMPREHENSIVE applications have been recommended for funding. Since the majority of investigators will be working in nonfederal hESC systems for the first time, a large number of them will want to be part of our teaching effort.

UCSF also has a long history of successfully collaborating with neighboring institutions. Modern science has to be a community effort, and the cumulative talent of Bay Area scientists is arguably the strongest in the nation. Thus far, 10 academic institutions have expressed their intent to participate in all three learning experiences we will offer (see letters in Part 1 of this application). They are the Gladstone Research Institutes, UC Berkeley, UC Santa Cruz, City College of San Francisco, San Francisco State University, Children's Hospital of Oakland Research Institute, San Dominican College of California, the California Institute for Quantitative Biological Research, California Pacific Medical Center Research Institute, and Blood Systems Research Institute.

To do the best possible job teaching hESC techniques to our colleagues, we need to renovate and equip as much space as possible to accommodate their needs. The additional funds will allow us to build-out another 613 sq. ft. that will consist of NONFEDERAL DERIVATION/hESC GROWTH & PROPAGATION RM 2, a SHARED TEACHING LABORATORY, a "TEACHING GREEN" DISCUSSION/INTERACTION AREA with a PRESENTATION ALCOVE and a PASS-THROUGH from our existing nonfederal area to the newly renovated space, which allows the transfer of human research materials. These areas are shown in green font on Attachment 2; for ease of viewing Attachment 4 includes a smaller version of the same plan and renderings of the individual areas. Please note that we will use our existing and newly renovated nonfederal space for teaching purposes, thereby achieving an economy of scale, as many functions and pieces of equipment will not have to be duplicated. +

Limit narrative to visible field area.



CIRM Shared Research Laboratory Information Form – Part Two

Section C. 1. Schedule and Drawdown of Funds Table (if applicable)

Provide a realistic schedule and drawdown of funds for completing each activity/milestone, as indicated below.

#	Activity/Milestone	Start Date	Completion or Milestone Date	Amount of CIRM funds to be drawn
1	Grant Award (estimate)		Jul 1, 2007	
2	Request for Planning Funds (10% of Construction Costs)		Jul 1, 2007	\$ 34,922
3	Prepare Preliminary Plans	Jul 9, 2007	Sep 10, 2007	
4	Approval of PPs		Sep 21, 2007	
5	Prepare Working Drawings	Sep 24, 2007	Dec 14, 2007	
6	Approval of WDs		Jan 11, 2008	
7	Request Construction Contract funds (80% of Construction Costs)		Dec 7, 2007	\$279,379
8	Advertise for Construction Contract	Jan 28, 2008	Feb 29, 2008	
9	Award Construction Contract		Mar 10, 2008	
10	Construction Activities	Mar 17, 2008	Aug 22, 2008	
11	Completion of Additional Equipment Purchases		May 26, 2008	
12	Request Additional Equipment Purchase funds		Jun 23, 2008	\$150,732
13	Beneficial Occupancy		Aug 22, 2008	
14	Notice of Completion		Aug 25, 2008	
15	Request Construction Completion Amount (10% of Construction Funding)		Sep 2, 2008	\$ 34,922

"Preliminary Plans" (PPs) represent approximately 35 percent of the design effort, or may be considered the product of completing the "Design Development" (DDs) phase of architectural work.

"Working Drawings" (WDs) represent drawings and specifications from which a contractor may determine the full extent of work contemplated in the project for purposes of submitting a bid; may be referred to as completion of "Construction Documents" (CDs) phase of architectural work.

"Additional Equipment" represents equipment to be used for the Stem Cell Techniques Course.



CIRM Shared Research Laboratory Information Form – Part Two

Section C. 2. Budget (if applicable)

Provide a complete budget for the additional renovation that includes construction costs, design fees, administration of the project, other costs (i.e. installation of equipment) and a construction contingency (limited to 7-10% of the construction budget). Identify the amount of CIRM funds requested and the matching funds (construction requires 20% matching funds). Provide a complete budget for additional movable equipment (equipment requires 20% matching funds). (narrative limited to 3 pages)

(Note: An Excel spreadsheet can be attached as long as the total submission for this Section is limited to 3 pages)

1. Renovation Budget

• Overview. In Section B.2, we justified our budget for renovation of the Shared Research Laboratory. Specifically, we proposed demolition of 1311 sq. ft. of space. If the research—but not teaching—portion of this grant is awarded, we will build-out only a portion of this space (698 sq. ft.), shown in blue font on Attachments 2 and 4, i.e., the NONFEDERAL DERIVATION/hESC GROWTH & PROPAGATION RM, NONFEDERAL hESC GROWTH & PROPAGATION RM 1 and GOWNING area. This area will be fully functional because it is connected to our existing nonfederal lab through an equipment room that was built as part of the recent lab renovation. The goal of this project is to add important capabilities with regard to hESC growth, propagation and derivation to our existing nonfederal laboratory, which was designed to house somatic cell nuclear transfer and research involving human embryos.

Here we describe our plans for renovating the entire space, another 613 sq. ft., which will be possible if both portions of our application are awarded. With the additional funds proposed in the teaching portion of the application, we will create (shown in green font on Attachments 2 and 4) NONFEDERAL DERIVATION/hESC GROWTH & PROPAGATION RM 2, a SHARED TEACHING LABORATORY, a “TEACHING GREEN” DISCUSSION/INTERACTION AREA and a PASS-THROUGH from our existing nonfederal area to the newly renovated space.

It is hard to overstate the importance of this renovation, not only to UCSF but to neighboring institutions. A very large number of researchers and trainees will need to use our space. Our vision is to run our teaching and research efforts simultaneously, which we think is the most cost-effective use of precious grant dollars that can be used for renovating space and purchasing equipment. For this reason, creation of a second tissue culture room for growing and propagating nonfederal hESCs will be a tremendous asset to us. This room, like its twin, can easily accommodate eight trainees and up to three instructors (see rendering, Attachment 4). Thus, our planned 4 weeks of formal instruction will not disrupt research activities, which will continue in NONFEDERAL hESC GROWTH & PROPAGATION RM 1. Finally, we note that both rooms have windows and sound systems that will allow viewers in the corridors to see and hear the activities that are going on without gowning and entering the room. This feature is important, as reducing foot traffic is a key element in preventing microbial contamination of hESCs.

In addition, we propose building other spaces that will greatly enhance the instructional portion of our program. The SHARED TEACHING LABORATORY is an open area where students can observe and practice techniques that are crucial elements of hESC research. In particular, this portion of the lab will contain stations where trainees will learn methods that are highly related to the activities going on in the nonfederal hESC growth, propagation and derivation rooms. For example, we will teach cryopreservation; the specialized equipment to carry out this procedure will be located in this area (see Attachments 2 and 4). Additionally, we will set up a processing area where cell samples will be prepared prior to advanced microscopic analyses, such as the methods that are used to assess markers of pluripotency or chromosome number. Teaching these techniques is an important part of the laboratory portion of our course and something we do almost daily. Finally, we propose locating the FACS machine in the SHARED TEACHING LABORATORY space. Sorting hESCs and their differentiated products by their physical and molecular characteristics is a fundamental technique in the field that nearly every researcher needs to understand.

The “TEACHING GREEN” DISCUSSION/INTERACTION AREA occupies the corridor outside the suite of hESC growth and derivation rooms (see rendering, Attachment 4). We envision that lively interchanges, similar to those that occur in the setting of a village green, will occur in this space. To facilitate these interactions, the north wall will be hung with large, white marker boards. The west wall of the corridor, THE PRESENTATION ALCOVE (see rendering, Attachment 4) will house a retractable projection screen for display of videos by a ceiling-mounted LCD projector. We plan to make a video library of the techniques we teach. If students see demonstrations of the methods they are about to learn, training times decrease drastically, with a commensurate increase in the depth of knowledge conveyed.

Finally, we propose creation of a PASS-THROUGH window that will directly connect the existing room that houses NONFEDERAL TISSUE CULTURE and the UCSF HUMAN GAMETE & EMBRYO BANK with the newly renovated area. This window will allow bank personnel to pass research materials, such as human embryos, directly to investigators working in the newly renovated area. This design, which is commonly used in in vitro fertilization clinics, is intended to minimize transit time and distance between the bank and the NONFEDERAL DERIVATION/hESC GROWTH & PROPAGATION RM.

• Itemization and justification. The budget we propose for the Shared Teaching Laboratory portion of this application is detailed in Attachment 5. As with the budget justification presented in Section B.2, line items are color-coded. The colors map to the categories listed in Section C.3, the Budget Summary Table (see legend at the bottom of the page). Together, these two



CIRM Shared Research Laboratory Information Form – Part Two

Section C. 2. Budget (continued)

documents constitute a detailed itemization of the costs that will be incurred.

As to the justification for the budget that is associated with the teaching portion of the application, we note that the dollars will be used to build-out the rest of the space that will be demolished as part of the renovation of the area described in the Shared Research Laboratory portion of this grant. Therefore, the sq. ft. costs are lower because they do not include demolition and shelling out of the space, which will be done as part of the construction project that will create the Shared Research Laboratory. In all other aspects, the same cost drivers that were described in Section B.2 also apply here.

However, we note the tremendous savings we will realize if the entirety of the demolished space is rebuilt at the same time. If the project is completed as a single phase of work, savings will be seen through reduced project administration costs, simplified design and bid packages, reduced bid and advertising costs, a single construction mobilization, economy-of-scale for construction materials and labor, a single demobilization, and minimization of cost escalation. In addition to cost saving and reducing the overall construction schedule, a single construction phase will reduce disruption to the adjacent newly renovated nonfederal laboratory by minimizing electrical and ventilation shutdowns, thereby reducing the risk of contamination, noise and vibration disruptions.

- **Institutional Match.** Since 2005, the UCSF School of Medicine has contributed \$518,000 (see appended letter from Dean David Kessler) and the Institute for Regeneration Medicine has donated \$560,000 (see appended letter from Director Arnold Kriegstein), which enabled creation of our existing nonfederal laboratory. We assigned one-third of this amount, \$356,000, as the “match” for the teaching portion of our application.

- **Benefit to California’s economy.** We note that the architectural and contracting firms chosen for this project will be California-based businesses.

2. Movable Equipment

- **Overview.** We propose purchasing equipment that will be installed in NONFEDERAL hESC GROWTH & DERIVATION RM 2. This room, a mirror image of NONFEDERAL hESC GROWTH & DERIVATION RM 1, also contains the exact same equipment. Please note that the large equipment items that will reside in the SHARED TEACHING FACILITY—the controlled-rate freezer and the FACS machine—are requested as part of the equipment purchase associated with our Shared Research Laboratory. If the teaching portion of our application is not funded, these items will be relocated to our existing nonfederal laboratory space.

- **Itemization and Justification.** The equipment that is part of our budget for the teaching part of this application is itemized in Table II. The justification for these items is described in Section B.2. Our need is driven by the very large numbers of users who want to take all of our courses—the formal and informal classes as well as instruction in hESC derivation.

Table II. Shared Teaching Laboratory: Movable Equipment

ITEM	QUANTITY	UNIT COST+TAX	TOTAL COST+TAX
hESC tissue culture hood (4 ft.)	3	\$ 8,840	\$ 26,520
hESC tissue culture incubator	6	\$ 8,940	\$ 53,640
Microscope (phase-contrast, with fluorescence and camera)	1	\$ 52,775	\$ 52,775
Fridge (“deli-style”)	1	\$ 3,600	\$ 3,600
Freezer –20°C(upright)	1	\$ 1,045	\$ 1,045
Centrifuge	1	\$ 13,152	\$ 13,152
Total -----			\$150,732

- **Institutional Match.** Since 2005, the UCSF School of Medicine has contributed \$283,628 for the purchase of key equipment that is housed in our current nonfederal space. The Dean’s office provided \$74,402 that allowed acquisition of specialized equipment that enables the manipulation of gametes and embryos (see appended letter from Dean Kessler). The Institute for Regeneration Medicine donated \$209,226 (see appended letter from Director Arnold Kriegstein), for a confocal microscope that allows us to take pictures of labeled molecules deep inside cells that are subsequently assembled into a three-dimensional picture. The details are given in Section B.4 (Institutional Commitment). One-third of this amount, \$93,597 was assigned to the teaching portion of this application.

- **Benefit to California’s Economy.** We will make every effort to purchase equipment from California-based companies.



CIRM Shared Research Laboratory Information Form – Part Two

Section C. 3. Budget Summary Table (if applicable)

Complete the budget summary for the use of CIRM funds.

Note: All colored fields contain calculated data. Please do not enter anything in those fields.

Other Project Costs				
Budget Category		Total Budget	CIRM Grant Funds	Institutional Match
Construction Contract Costs		\$ 222,902	\$ 222,902	\$ 000
Other Construction Costs (institutional)		\$ 21,715	\$ 21,715	\$ 000
Subtotal Construction		\$ 244,617	\$ 244,617	\$ 000
Design Fees		\$ 48,839	\$ 48,839	\$ 000
Administrative Costs		\$ 31,006	\$ 31,006	\$ 000
Construction Contingency		\$ 24,762	\$ 24,762	\$ 000
Total Construction		\$ 349,224	\$ 349,224	\$ 000
Additional Movable Equipment		\$ 150,732	\$ 150,732	\$ 000
Total Budget		\$ 499,956	\$ 499,956	\$ 000
Gross Square Feet	613	\$ 569.70	\$ 569.70	Const Costs/GSF
Assignable Square Feet	555	\$ 629.23	\$ 629.23	Const Costs/ASF



CIRM Shared Research Laboratory Information Form – Part Two

Section D. Signature Page

Complete, save, and print Part Two of the Shared Research Laboratory Grant Information.

Submit electronic application as an email attachment to laboratory@cirm.ca.gov no later than 5:00pm PST on March 16, 2007.

Mail* the original executed Part Two application and five (5) copies to:

Shared Research Laboratory Grant Application

California Institute for Regenerative Medicine

210 King Street

San Francisco, CA 94107

***Mailing must be postmarked no later than March 16, 2007.**

Applications will not be accepted after these deadlines.

Project Start Date

Jul 1, 2007

Construction Start Date

Oct 29, 2007

Occupancy Date

Aug 22, 2008

Total Part Two Funds Requested for Shared Laboratory Space

\$1,999,692

Total Part Two Funds Requested for Stem Cell Techniques Course

\$ 499,956

Total Capital Funds Requested

\$1,349,127

Facilities Contact

Mr. Michael Bade
Director, Capital Programs
Capital Projects & Facilities Management
University of California, San Francisco
3130 20th Street
Box 0894
San Francisco, CA 94143
(415) 502-6460
mbade@fm.ucsf.edu

Authorized Organizational Official

Date

Print Name

Title

Program Director

Date

Print Name

Title



CIRM Shared Research Laboratory Information Form – Part Two Supplement

Project Information

Application Number

Program Director Name:

Historical Performance

Provide information on past performance for 3 projects.

	Project 1	Project 2	Project 3
Brief Project Title	HSE 16th Fl. DSCB Ren.	HSE 14th Fl. Partial Ren	MSB 10th fl. Ren.
Original Budget (Total project cost)	\$3,869,668	\$4,946,290	\$1,070,300
Final project cost	\$3,869,668	\$4,946,290	\$1,070,300
Scheduled Completion Date	Sep 19, 2006	Jul 14, 2006	Nov 4, 2006
Actual Notice of Completion Date	Oct 10, 2006	Jul 21, 2006	Nov 4, 2006
Gross Square Feet involved	6,143	7,400	1,400
Assignable Square Feet involved	4,720	6,660	1,301
Approximate number of change orders	8	8	3
Value of all change orders & claims	\$ 187,733	\$ 267,211	\$ 83,200
Type of construction management	In-house Forces	Design-Bid-Build	Design-Bid-Build

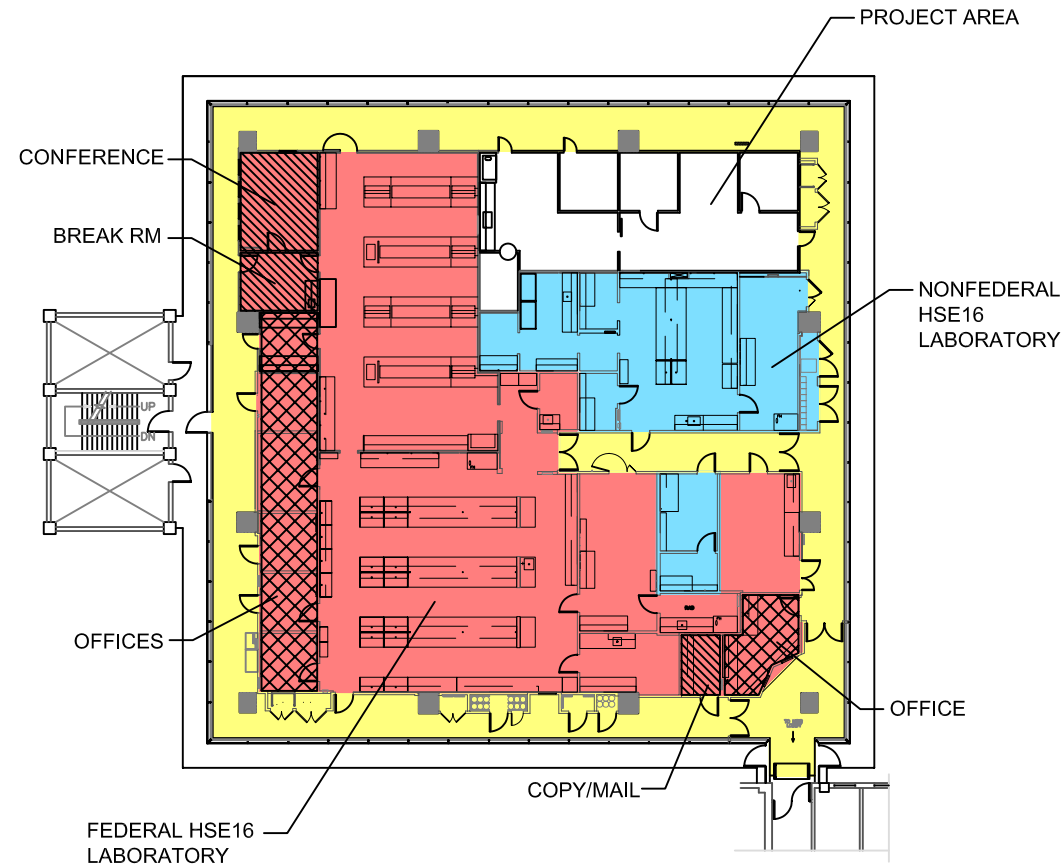
Laboratory Alteration Projects

Please enter the number of laboratory alteration projects completed by the applicant in the past 2 years (in the range of \$1-5 million in project cost), and the approximate total dollar value that these projects represent.

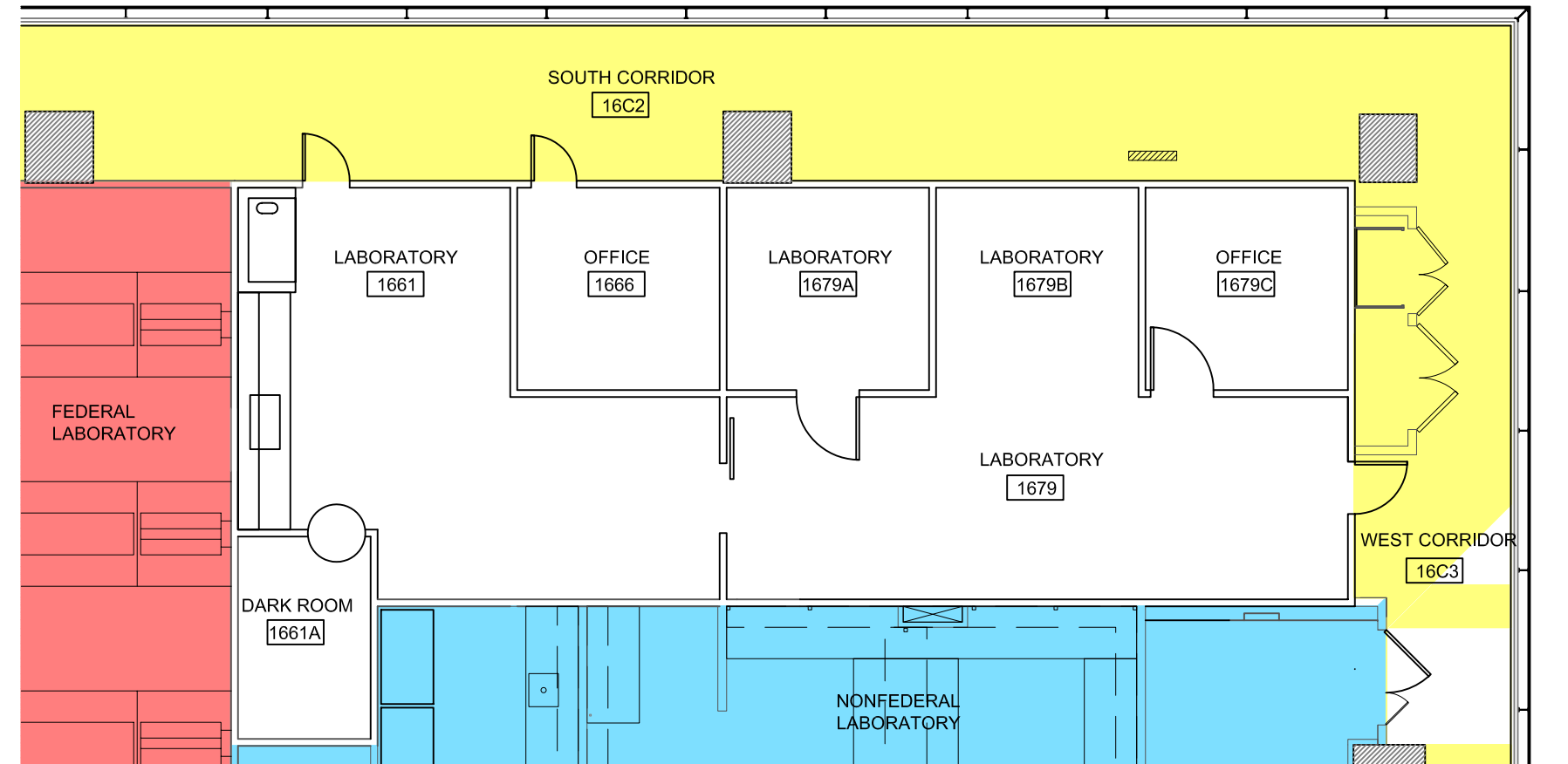
Total Laboratory Alteration Projects

Approximate Total Value

Limit Budget Justification to visible field area.



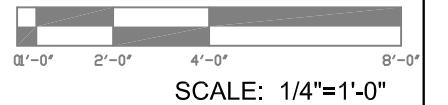
HSE 16TH FLOOR- EXISTING REFERENCE PLAN SCALE: 1/32"=1'-0"



HSE 16TH FLOOR- EXISTING REFERENCE PLAN

SCALE: 1/8"=1'-0" 0'-0" 4'-0" 8'-0" 16'-0"





PROJECT BUDGET WORKSHEET

CAPITAL PROGRAMS & FACILITIES MANAGEMENT- Box 0894

HSE 16 Nonfederal CIRM Shared Research & Teaching
Project Title: Facility
Project No. M6439

1. CONSTRUCTION:

- a. General Construction.
- b. Facilities Management Construction (Breakdown on next page)
- c. Campus Construction (Breakdown on next page)
- d. Construction Contingency (10% of a,b,c,g,h)
- e. Asbestos Construction
- f. Asbestos Construction Contingency (10% of e)
- g. Supplemental Construction Inspection
- h. Other - Special Inspections

Total Construction:

2. UTILITIES:

3. INVENTORIAL EQUIPMENT:S/M Gr. 2 & 3 Equip.

4. LANDSCAPING & SITE DEVELOPMENT:

5. DESIGN SERVICES:

- a. Design Consultants
- b. AD&E Design Services
- c. Fire Protection Consultants
- d. Construction Management Consultants
- e. Engineering Consultants
- f. Special Inspection (IOR)
- g. Plan Review
- h. Other

Total Design Services:

6. PROJECT MANAGEMENT:

- a. Major Projects Manager Services
- b. Major Projects Relocation Services
- c. UA&P Project Planning Guide (PPG)
- d. Other

Total Project Management:

7. SURVEYS, TESTS, PRINTING & ADVERTISING:

- a. Site & Topo Surveys
- b. Testing
- c. Printing (Specifications, Blueprints)
- d. Advertising
- e. Messenger
- f. Reimbursables (Design)
- g. Reimbursables (AD&E)
- h. Agency Fees (DSA, OSHPD, SFM)
- i. Builders Risk Insurance
- j. Other

Total Surveys, Tests, Printing & Adv.:

8. CAMPUS/SPECIAL ITEMS:

- a. EH&S Services
- b. Furniture
- c. Moving Carrier
- d. E.N.S. (Data/Telecommunications)
- e. Other

Total Special Items:

9. PROJECT CONTINGENCY (10% of subs 2-8):

GRAND TOTAL:

Plant Acct. No.:	927840		
Project Mgr.:	Patti Mitchell	14-Mar-07	
Funded By:	S/M		
HSE 16 CIRM Suite Total Budget	Shared Research Laboratory	Shared Teaching Laboratory	
\$829,582	\$611,320		\$218,262
\$42,469	\$30,954		\$11,515
\$0	\$0		\$0
\$83,470	\$59,472		\$23,998
\$21,151	\$16,511		\$4,640
\$2,315	\$1,551		\$764
\$0	\$0		\$0
\$46,419	\$36,219		\$10,200
\$1,025,406	\$756,027		\$269,379
\$0	\$0		\$0
\$0	\$0		\$0
\$0	\$0		\$0
\$165,000	\$122,500		\$42,500
\$25,270	\$18,931		\$6,339
\$2,200	\$1,474		\$726
\$192,470	\$142,905		\$49,565
\$56,000	\$46,000		\$10,000
\$15,000	\$10,850		\$4,150
\$2,500	\$1,675		\$825
\$73,500	\$58,525		\$14,975
\$400	\$268		\$132
\$5,000	\$3,600		\$1,400
\$5,000	\$3,600		\$1,400
\$251	\$168		\$83
\$4,875	\$3,516		\$1,359
\$0	\$0		\$0
\$6,000	\$4,320		\$1,680
\$800	\$536		\$264
\$22,326	\$16,008		\$6,318
\$5,495	\$3,932		\$1,563
\$500	\$335		\$165
\$5,995	\$4,267		\$1,728
\$29,429	\$22,171		\$7,259
\$1,349,127	\$999,903		\$349,224

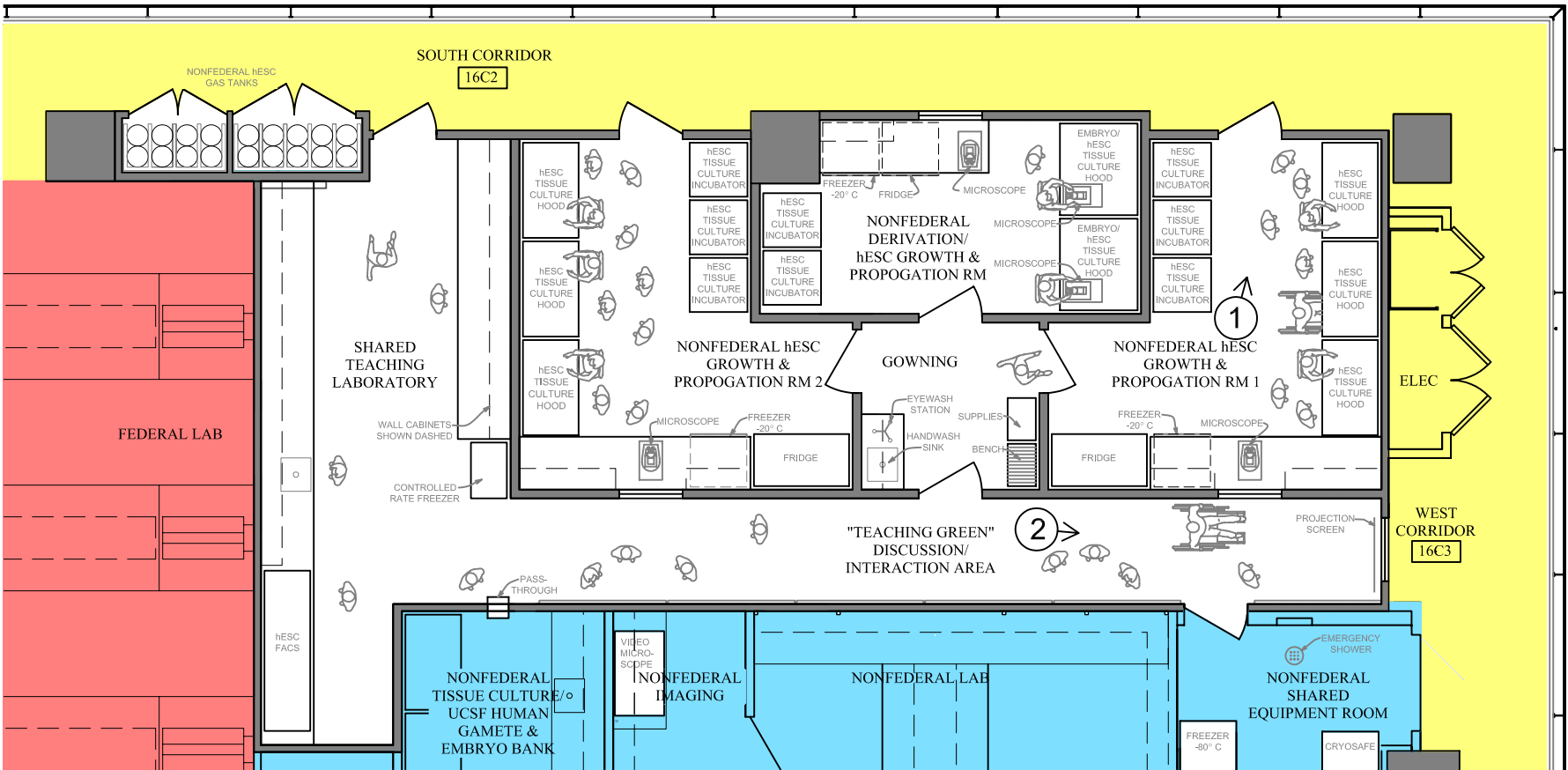
Cost Legend - Shared Research Laboratory

Construction Contract Costs	\$627,831
Other Construction Costs (Institutional)	\$67,173
Design Fees	\$141,431
Administrative Costs	\$102,445
Construction Contingency	\$61,023



ARTIST'S RENDERING: PROPOGATION ROOM

①



FLOOR PLAN: PROPOSED NONFEDERAL SHARED RESEARCH LAB & STEM CELL TECHNIQUES TEACHING LAB



ACCESS TO VIEW



PRESENTATION ALCOVE



ARTIST'S RENDERING: "TEACHING GREEN" DISCUSSION/INTERACTION AREA

②



PROJECT BUDGET WORKSHEET

CAPITAL PROGRAMS & FACILITIES MANAGEMENT- Box 0894

HSE 16 Nonfederal CIRM Shared Research & Teaching
Project Title: Facility
Project No. M6439

Plant Acct. No.:	927840
Project Mgr.:	Patti Mitchell 14-Mar-07
Funded By:	S/M

	HSE 16 CIRM Suite Total Budget	Shared Research Laboratory	Shared Teaching Laboratory
1. CONSTRUCTION:			
a. General Construction.	\$829,582	\$611,320	\$218,262
b. Facilities Management Construction (Breakdown on next page)	\$42,469	\$30,954	\$11,515
c. Campus Construction (Breakdown on next page)	\$0	\$0	\$0
d. Construction Contingency (10% of a,b,c,g,h)	\$83,470	\$59,472	\$23,998
e. Asbestos Construction	\$21,151	\$16,511	\$4,640
f. Asbestos Construction Contingency (10% of e)	\$2,315	\$1,551	\$764
g. Supplemental Construction Inspection	\$0	\$0	\$0
h. Other - Special Inspections	\$46,419	\$36,219	\$10,200
Total Construction:	\$1,025,406	\$756,027	\$269,379
2. UTILITIES:	\$0	\$0	\$0
3. INVENTORIAL EQUIPMENT:S/M Gr. 2 & 3 Equip.	\$0	\$0	\$0
4. LANDSCAPING & SITE DEVELOPMENT:	\$0	\$0	\$0
5. DESIGN SERVICES:			
a. Design Consultants	\$165,000	\$122,500	\$42,500
b. AD&E Design Services			
c. Fire Protection Consultants			
d. Construction Management Consultants			
e. Engineering Consultants	\$25,270	\$18,931	\$6,339
f. Special Inspection (IOR)			
g. Plan Review	\$2,200	\$1,474	\$726
h. Other			
Total Design Services:	\$192,470	\$142,905	\$49,565
6. PROJECT MANAGEMENT:			
a. Major Projects Manager Services	\$56,000	\$46,000	\$10,000
b. Major Projects Relocation Services	\$15,000	\$10,850	\$4,150
c. UA&P Project Planning Guide (PPG)	\$2,500	\$1,675	\$825
d. Other			
Total Project Management:	\$73,500	\$58,525	\$14,975
7. SURVEYS, TESTS, PRINTING & ADVERTISING:			
a. Site & Topo Surveys			
b. Testing	\$400	\$268	\$132
c. Printing (Specifications, Blueprints)	\$5,000	\$3,600	\$1,400
d. Advertising	\$5,000	\$3,600	\$1,400
e. Messenger	\$251	\$168	\$83
f. Reimbursables (Design)	\$4,875	\$3,516	\$1,359
g. Reimbursables (AD&E)	\$0	\$0	\$0
h. Agency Fees (DSA, OSHPD, SFM)	\$6,000	\$4,320	\$1,680
i. Builders Risk Insurance	\$800	\$536	\$264
j. Other			
Total Surveys, Tests, Printing & Adv.:	\$22,326	\$16,008	\$6,318
8. CAMPUS/SPECIAL ITEMS:			
a. EH&S Services	\$5,495	\$3,932	\$1,563
b. Furniture			
c. Moving Carrier			
d. E.N.S. (Data/Telecommunications)	\$500	\$335	\$165
e. Other			
Total Special Items:	\$5,995	\$4,267	\$1,728
9. PROJECT CONTINGENCY (10% of subs 2-8):	\$29,429	\$22,171	\$7,259
GRAND TOTAL:	\$1,349,127	\$999,903	\$349,224

Cost Legend - Shared Teaching Laboratory

Construction Contract Costs	\$222,902
Other Construction Costs (Institutional)	\$21,715
Design Fees	\$48,839
Administrative Costs	\$31,006
Construction Contingency	\$24,762



Appendix A

Application: CL1-00523-1

Title: The University of California San Francisco Shared Research and Teaching Laboratory: a Non-Federal Human Embryonic Stem Cell Resource for the Bay Area Community

Public Abstract:

The University of California, San Francisco (UCSF) has a long history of making innovative discoveries that change the way scientists and clinicians think about disease processes and their approaches to finding cures. Accordingly, researchers at this institution were quick to appreciate the enormous promise of human embryonic stem cells (hESCs) as research tools for understanding how the body normally works, thus laying the groundwork to identify disease-related aberrations. Therefore, in 2001, when the federal government decided to limit government funding to work with existing hESCs, which they banked, U.S. scientists were faced with a dilemma. Would we abide by these unprecedented restrictions, which meant that research would be limited to first-generation cells, or could we find ways to develop second-generation, higher-quality hESCs? Investigators on our applicant team took both approaches. Since UCSF contributed two hESC lines to the federal registry, our team members participated in the government's program to distribute these cells, which entailed teaching scientists how to use them. We also sought nonfederal funding sources to derive new hESC lines. Thus, we have a great deal of experience that is directly relevant to achieving the California Institute for Regenerative Medicine's (CIRM's) goal of establishing Shared Research Laboratories that also offer hands-on courses. We give the highest priority to teaching hESC techniques in the context of the ethical issues surrounding this work.

Here, we propose to expand the nonfederal laboratory space that already exists at UCSF. Renovating and equipping an adjacent lab will significantly increase our capacity for growing and analyzing second and subsequent generations of hESCs. Our goal is to make the existing space, renovated with UCSF funds, and the new lab to be created with this CIRM award, available to our colleagues. We also want to jump-start their work by teaching them how to grow and analyze hESCs. Thus far, 16 graduate- and postgraduate trainees are funded by our CIRM training grant; 32 UCSF scientists have applied for CIRM SEED and Comprehensive grants, and we expect many more will follow. We also want to support the work of our colleagues at 10 neighboring institutions. At the same time, we will use this lab to derive new and higher-quality hESC lines. We will also teach these techniques to highly motivated California scientists. Our work is important because the researchers who use our laboratory are studying the causes of major human diseases that occur as the result of trauma (e.g., paralysis), cell death (e.g., Parkinson's and Alzheimer's diseases, diabetes, cardiac failure), or cell malfunction (e.g., cancer). Thus, by sharing our laboratory space, scientific equipment and technical expertise with colleagues at UCSF and other institutions, we will play an important role in helping scientists accomplish CIRM's ultimate goal of finding cures for human diseases.

Statement of Benefit to California:

By voting in favor of Proposition 71, which funds research involving human embryonic stem cells (hESCs) that is not supported by the federal government, the citizens of California sent a clear message that they want scientists in our state to play an important role in research that could revolutionize medical treatments and render significant economic benefits. Currently, these treatments largely consist of surgical or pharmacological interventions, and transplantation approaches that involve significant hurdles. For example, human cells carry unique identifiers—molecular “bar codes”—that must be closely matched or the transplant will be rejected. And, unless the bar codes match perfectly, the recipient has to take powerful drugs to suppress rejection. Finally, there are major shortages of cells and organs for use in transplantation procedures. With the advent of hESCs, researchers are envisioning new therapeutic approaches. In theory, these cells, the building blocks of the entire body, can become any cell type. Thus, there is a great deal of excitement about using hESC-based transplantation techniques to cure human diseases.

Why haven't these approaches moved forward full throttle? In 2001 the federal government limited hESC research to existing cell lines. This unprecedented move created additional barriers. If scientists want to make new hESC lines or work with higher-quality cells that were established after 2001, they have to use labs that are completely devoid of government funding—that means building materials, equipment and supplies. Therefore, these labs must be created with funds from nonfederal sources, one of the reasons that the California Institute for Regenerative Medicine was created. We envision that our proposed Shared Research Laboratory and Teaching Facility will help us create a major center for conducting the most exciting aspects of hESC research that will ultimately lead to cures for many of the most devastating human diseases.